REMARKS

This is in response to the Office Action mailed December 13, 2004. A Petition for an extension of time and check therefor accompanies this response.

Claims 1 to 15 are in this application. Applicant confirms election of claims 6 to 11. Claims 1 to 5 and 12 to 15 are withdrawn from consideration.

Claim Objections/Rejections 35 U.S.C. 112

In this amendment, claims 6 to 11 have been amended to address the Examiner's claim objections and the claim rejections under 35 U.S.C. 112, second paragraph. It is submitted that these amendments are self-explanatory and clearly address the Examiner's concerns. No amendment has been made to the term "fluorescenated conjugate" and it submitted that this phrase is proper and definite taking into account the disclosure in the specification and the fact that one skilled in the art would clearly understand the term. The Examiner is requested to reconsider the rejection under 35 U.S.C. 112, second paragraph, of this term.

In view of the above, withdrawal of the objections and rejections under 35 U.S.C. 112, second paragraph, of the claims

is respectfully requested.

Claim rejections under 35 U.S.C. 103

Claims 6 to 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen in view of McHugh, Ngo, Victor, and Schwartz. The Examiner's reasons for this rejection are set out on paragraph 18 of the office action. The Applicant respectfully disagrees with the Examiner's conclusions reflating to the cited art and offers the technical discussion below in an effort to have the Examiner withdraw this rejection.

As a general point of introduction, the term or usage of the words "antigen or antibody" should be appreciated. The claimed bead may contain (i.e. be coated with) antigens to specific bacterial/viral proteins. That system is then used to capture (or detect) certain bacterial/viral antibodies. However, once a "detector" antibody (e.g. goat anti-human IgG FITC, etc.) is utilized for the purpose of identifying the presence of bound antibody to that specific antigen, the "detector" antibody itself is looking for a specific antigen which, in this case, is another antibody. These terms may often be interchangeable depending on their usage.

Hansen describes a process unlike anything in the present

invention. Hansen utilizes the process of agglutination of beads to create complexes of 2, 3, or more *clumps* and distinguishes them by their scatter properties. This is really a part of the difficulties encountered in the early stages of bead based assays, namely, investigators had real problems with bead *clumping* and had to live with it as an analytical tool. The presently claimed invention has virtually eliminated or substantially reduced the clumping issue and uses *pure scatter properties* to distinguish the bead populations. Applicant is able to discretely separate individual, single bead sizes because of the unique properties of the coating and analysis procedures.

Quoting from Hansen: "the present invention relates to optical analytical methods based on rates of particle agglutination" (see column 1, lines 10 to 12). Hansen uses (Ab)-antigen. "A" is present in solution, and it will couple beads containing antibodies to antigen "A" forming a bead complex. Likewise, the same is true for the detection of antibodies in samples to antigens.

The Examiner mentions that this invention is a "no-wash" system and questions why there is washing in the initial portions of the application. In this regard, it is emphasized that the part that the Examiner is referring to is the *manufacturing*

procedure and does require washings to elute-off any excess antigens not bound to the surface of the beads. There are no washing steps in the actual analytical portion of the invention (i.e. use of the kit/assay as opposed to the manufacture thereof).

Fulwyler and McHugh: Applicant has developed a manner of coating the beads which is unique and different to the procedures in Fulwyler. These differences can be summarized as set forth below:

(1) Applicant does not use PBS at pH 7.0 or Tris Buffer pH 8.4. Even though buffer in appendix states making carbonate buffer pH 9.5, Applicant's is bicarbonate and carbonate specialized mixtures.

(2) Applicant does not need PBS-BSA-Tween to wash the beads. This generally is used to prevent clumping. Applicant has beads formulated prior to coating that eliminates this problem.

(3) Applicant's invention requires only a protein/bead incubation in the refrigerator for 12 - 18 hours. No pre-incubation is required as in Fulwyler at 37 degrees for 3 hours.

(4) No 37 degree incubation for 1 hour for blocking is required in the present invention. Applicant's invention is one wash step with a low percentage of BSA in carbonate buffer.

(5) Storage - Applicant does not need to store beads in solutions containing glycerol. Further, Applicant does not need to pre-wash the beads prior to usage.

(6) Applicant's invention is a "no-wash" assay (i.e. no washes between incubation steps) which is not the case with Fulwyler.

In summary, this invention is far advanced from any patent or article published and uses techniques that are not obvious to the user. It has taken time and creative technical skill to develop a system unlike any currently cited. Extensive research has gone into the types of beads, optimizing the percentage of surfactants in the storage medium, and optimal binding conditions for each type of antigen/antibody reaction. Furthermore, the ability to prevent the beads from clumping (i.e. forming complexes of 2 or more beads) is difficult to achieve and different from any of the other procedures mentioned. Applicant's invention has accomplished a way to virtually eliminate this phenomenon, unlike Hansen's patent whose entire premise is base

on agglutination.

Hansen utilizes light scatter properties to detect the aggregates of the beads. This only implements two of the possible analysis channels found in modern flow cytometers. Hansen also uses a "Delta" difference in the refractive index between reactions occurring in the bead signals to determine differences, or variations, of the singlets versus the doublets and triplets or multiplexes of beads. This "Delta" is the measure of positivity. The present invention uses size discrimination for separating each bead and then fluorescent markers to detect the presence or absence of the specific binding of the antigen or antibody to the bound antigen or antibody, respectively. Hansen has limitations on the number of assays performed in one tube because of the interference agglutination may cause using multiple sized beads. The present invention uses discrete sizes which are easily recognizable and, therefore, have the ability to separately be distinguished one bead assay from the other. This greatly facilitates user operation and interpretation.

Ngo, et. al. teaches a solid phase system by which one could only utilize one stationary test tube with either a fluorescent or RIA technology. Multiple washes are necessary. Ngo does teach a technique conducive to clinical laboratory testing. Competitive

binding is the key difference in this solid state technology expressed by Ngo. Flow has "free-floating" beads which are suspended in a medium and analyzed by passing through a quartz flow cell and counted as a single particle. Ngo counts the development of the supernatant in either radioactive counts or fluorescent intensity at a static state.

Victor: The Examiner in this example is referencing a technique that is similar to the immuoblot systems of the past. Antigens are impregnated onto membrane strips, incubated with patient sample, and developed using dyes, radioisotopes or other markers. This is neither a flow cytometric method nor is it close to having the clinical advantages outlined in the present invention.

Schwartz's beads are well known in the flow cytometric community. However, they are strictly fluorescent beads of different intensities used to calibrate flow cytometers and determine if they are linear in their reportable results. Most users rely on Schwartz's beads for alignment of the instruments and not on clinical results. The present invention is clinical in nature in that it provides the clinician with a diagnostic result used in the treatment of patients.

Double Patenting Rejection

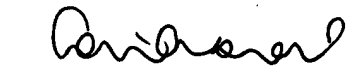
Claims 6 to 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 to 12 of U.S. Patent No. 6,159,748. The Examiner correctly acknowledges that the claims are not identical, but incorrectly holds that t hey are not patentable distinct from each other. It is hoped that the technical discussion above will convince the Examiner that the claims in the present application are distinct from the claim in the cited patent. In ay event, it is respectfully requested that this matter be held in abeyance (if the Examiner should continue to maintain the double patenting rejection) pending the resolution of allowable claims in this application.

It is submitted that this response addresses all of the concerns and issues raised by the Examiner in the office action, and that the amendments and technical discussion herein provides justification for the allowance of all the claims pending in this application. In this regard, the Examiner is requested to note that the claimed invention recites a series of steps in a arranged order and the claimed invention should be considered as such when evaluating it against the references cited. With this in mind, favorable reconsideration and allowance of all the claims would be proper in the circumstances.

If the Examiner has any questions or further concerns, he is invited to contact the undersigned at telephone number (818)710-2788.

Please acknowledge safe receipt of this Response by stamping and returning the enclosed postcard.

Respectfully submitted,



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Enclosed: Petition for extension
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on June 13, 2005.

Colin P. Abrahams

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